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Brief Clinical Report

Lethal Neonatal Mandibuloacral Dysplasia

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We report on a case of lethal neonatal mandibuloacral dysplasia. Large confluent fontanelles, sparse fine hair and eyebrows, pseudo-exophthalmos, micrognathia, bulbar digits, and short clavicles were present. In addition, we describe for the first time the presence of glandular hypospadias in this disorder. We propose that this neonatally lethal case represents severe expression of mandibuloacral dysplasia.

KEY WORDS: progeroid, mandibuloacral dysplasia, Wiedemann-Rautenstrauch

INTRODUCTION

We report on a case of mandibuloacral dysplasia neonatally evident. This condition has most often been reported in individuals of Italian descent [Tenconi et al., 1986].

CLINICAL REPORT

The propositus was born to healthy nonconsanguineous, non-Italian South African caucasoid parents. The couple have two healthy boys and had a history of two first trimester miscarriages of unknown cause.

Unexplained mild polyhydramnios characterized the pregnancy and the term male infant had a birthweight of 2,640 g, crown-heel length of 49 cm, head circumference of 35 cm, and thin, transparent, and parchment-like skin, with easily visible veins most prominent over the scalp. There was little subcutaneous fat with the exception of the cheeks. Hair and eyebrows were fine and sparse. Eyelashes were short. Capillary hemangiomata were noted over the eyelids, glabellar area and nape of neck (Fig. 1). One 10 × 4 mm café-au-lait mark was present in the left subareolar region.

The anterior fontanelle was large (90 × 70 mm) and communicated by a 40 mm wide sagittal suture with the 90 × 50 mm posterior fontanelle (Fig. 2). The palpebral fissures were horizontal to down-slanting. The eyes were mildly prominent and the malar areas hypoplastic. No cataracts were noticed. The ears were apparently low-set with small narrow lobes. The nose was

Fig. 1. Sparse eyebrows and capillary hemangiomata.

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Fig. 2. Autopsy showing large confluent fontanelles.

Fig. 3. Note micrognathia, narrow ear lobes and fine sparse hair.

Fig. 4. Note the "bulbar" terminal phalanges and the beaked nails.

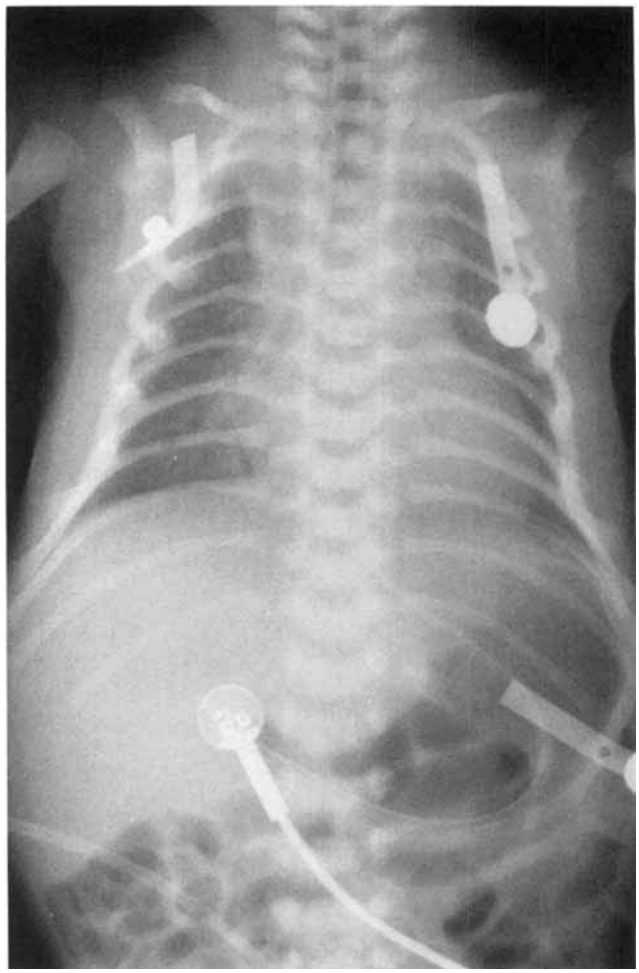

Fig. 5. The chest film demonstrates a bell-shaped chest and short clavicles.

prominent and thin with a well-formed bridge. The cheeks were bulbous. Micrognathia was striking (Fig. 3). The mouth opening was small and the upper lip thin. The palate was high arched, with no clefting. The alveolar margins were irregular.

The shoulders sloped. The fingers were long and showed ulnar deviation; they had shortened bulbous terminal phalanges covered by tense, translucent skin. The nails were convex and beaked (Fig. 4). Glandular hypospadias and right cryptorchidism were present.

X-rays films showed a bell-shape chest and clavicular hypoplasia (Fig. 5), as well as mandibular hypoplasia. No wormian bones were visible. Unfortunately, roentgenograms of the digits were not available. The long bones showed mild bowing. Chromosomes were apparently normal (46,XY). The patient had apnoeic episodes and died 8 days after birth. No pathology of the internal organs was identified at autopsy. Unfortunately, no histology of the skin was carried out. Fibroblast cultures were established and collagen studies are being planned.

DISCUSSION

This infant had large confluent fontanelles, sparse fine hair and eyebrows, pseudo-exophthalmos, micrognathia, bulbar digits, and short clavicles consistent with mandibuloacral dysplasia. This is the first report of a congenital case. Le Merrer et al. [1991] described a 2-year-old, who may have had congenital manifestations; the sib of this case was affected at birth and died soon thereafter (Le Merrer, personal communication). This supports autosomal recessive inheritance.

Glandular hypospadias has not been described previously in mandibuloacral dysplasia. This case represents a severe neonatal and lethal form of mandibuloacral dysplasia. We propose that despite the usual pattern of postnatal onset/recognition, mandibuloacral dysplasia should be considered in the differential diagnosis of infants with such features.

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REFERENCES

Le Merrer M, Guillot M, Briard M-L, Maroteaux P (1991): Lethal progeroid syndrome with osteolysis. Case Report. Ann Génét (Paris) 34:82–84.

Tenconi R, Miotti F, Miotti A, Audino G, Ferro R, Clementi M (1986): Another Italian family with mandibuloacral dysplasia: Why does it seem more frequent in Italy? Am J Med Genet 24:357–364.